

**We Claim:**

1. An isolated polypeptide comprising 42 or more contiguous amino acids from an amino acid sequence selected from SEQ ID NOs: 2 and 12.
- 5 2. An isolated polypeptide comprising an amino acid sequence selected from SEQ ID NOs: 2 and 12.
3. An isolated polynucleotide encoding a polypeptide of claim 1.
- 10 4. An isolated polynucleotide comprising a nucleotide sequence selected from SEQ ID NOs: 1 and 11.
5. A recombinant vector comprising the polynucleotide of claim 3.
- 15 6. A host cell comprising the vector of claim 5.
7. An antibody which specifically binds to a polypeptide of claim 1.
8. An antibody which specifically binds to a polypeptide comprising an amino acid  
20 sequence selected from SEQ ID NOs: 39-42.
9. A method for making a polypeptide comprising culturing a host cell of claim 6 under conditions in which the nucleic acid is expressed.
- 25 10. The method of claim 9 wherein the polypeptide is isolated from the culture.
11. A method for identifying an antagonist of NPC1L1 comprising:
  - (a) contacting a host cell expressing a polypeptide comprising an amino acid sequence selected from SEQ ID NOs: 2, 4 and 12 or a functional fragment thereof on a  
30 cell surface, in the presence of a known amount of detectably labeled ezetimibe, with a sample to be tested for the presence of the antagonist; and
  - (b) measuring the amount of detectably labeled ezetimibe specifically bound to the polypeptide;

wherein an NPC1L1 antagonist in the sample is identified by measuring substantially reduced binding of the detectably labeled ezetimibe to the polypeptide, compared to what would be measured in the absence of such an antagonist.

5 12. A method for identifying an antagonist of NPC1L1 comprising:

(a) placing, in an aqueous suspension, a plurality of support particles, impregnated with a fluorescer, to which a host cell expressing a polypeptide comprising an amino acid sequence selected from SEQ ID NOs: 2, 4 and 12 or a functional fragment thereof on a cell surface are attached;

10 (b) adding, to the suspension, radiolabeled ezetimibe and a sample to be tested for the presence of the antagonist, wherein the radiolabel emits radiation energy capable of activating the fluorescer upon the binding of the ezetimibe to the polypeptide to produce light energy, whereas radiolabeled ezetimibe that does not bind to the polypeptide is, generally, too far removed from the support particles to enable the radioactive energy to  
15 activate the fluorescer; and

(c) measuring the light energy emitted by the fluorescer in the suspension;

wherein an NPC1L1 antagonist in the sample is identified by measuring substantially reduced light energy emission, compared to what would be measured in the absence of such an antagonist.

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13. The method of claim 12 wherein the fluorescer is selected from yttrium silicate, yttrium oxide, diphenyloxazole and polyvinyltoluene.

14. A method of claim 11 wherein the ezetimibe is labeled with a radiolabel selected  
25 from  $^3\text{H}$  and  $^{125}\text{I}$ .

15. A method of claim 12 wherein the ezetimibe is labeled with a radiolabel selected from  $^3\text{H}$  and  $^{125}\text{I}$ .

30 16. A method for identifying an antagonist of NPC1L1 comprising:

(a) contacting a host cell expressing a polypeptide comprising an amino acid sequence selected from SEQ ID NOs: 2, 4 and 12 or a functional fragment thereof on a cell surface with detectably labeled cholesterol and with a sample to be tested for the presence of the antagonist; and

35 (b) measuring the amount of detectably labeled cholesterol in the cell;

wherein an NPC1L1 antagonist in the sample is identified by measuring substantially reduced detectably labeled cholesterol within the host cell, compared to what would be measured in the absence of such an antagonist.

5     17 . The method of claim 16 wherein the cholesterol is detectably labeled with a radiolabel selected from  $^3\text{H}$  and  $^{125}\text{I}$ .

18. A method according to claim 11 wherein the host cell is selected from a chinese hamster ovary (CHO) cell, a J774 cell, a macrophage cell and a Caco2 cell.

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19. A method according to claim 12 wherein the host cell is selected from a chinese hamster ovary (CHO) cell, a J774 cell, a macrophage cell and a Caco2 cell.

20. A method according to claim 16 wherein the host cell is selected from a chinese  
15 hamster ovary (CHO) cell, a J774 cell, a macrophage cell and a Caco2 cell.

21. A mutant mouse comprising a homozygous disruption of endogenous, chromosomal *NPC1L1* wherein the mouse does not produce any functional NPC1L1 protein.